REMARKS

Reconsideration of the rejections set forth in the Office action dated February 19, 2010 is requested. Claims 1-18 are pending and under consideration.

I. Interview Summary

Applicants thank Examiner Young for the courtesy of an interview on May 17, 2010. Compliant with M.P.E.P. § 713.04, Applicants provide this summary of the interview. Examiner Young and Applicants' representatives, Judy Mohr and Susan Harlocker, discussed the clarifying amendment to claim 1 that is presented in this amendment and, briefly, the cited art. The Examiner agreed that the amendment presented herein is consistent with his understanding of the claim as searched and examined thus far, and agreed to enter this amendment for clarification of the claim prior to appeal.

II. Amendments

Claim 1 is amended to grammatically clarify the functional features of the polymer that forms the polymer film deposited on the unitary body. This amendment is consistent with the remarks on the record (see, for example, Applicants' response filed Nov. 9, 2009, page 8, Section C1), and places the rejected claims in better form for consideration on appeal, and therefore is compliant with 37 C.F.R. § 1.116.

III. Rejections Under 35 U.S.C. § 103(a)

Claims 1-18 remain rejected as allegedly obvious in view of Johnson *et al.* (U.S. 6,171,618, hereafter "the '618 patent").

A. The Pending Claims.

The present claims are directed to a method of manufacturing an oral dosage form, comprising, in part, dispersing a second drug in a solid matrix to form a unitary body which upon immersion in a gastrointestinal fluid releases the second drug by prolonged release, depositing on a surface of the unitary body a polymeric film formed from a polymer which dissolves in gastrointestinal fluid upon ingestion.

B. The Cited Art

The '618 patent discloses dosage forms designed for the sustained release of two drugs, pseudoephedrine and cetirizine (Col. 1, lines 56-64). Sustained release is achieved by two different dosage form designs. The first dosage form design is described on Col. 2, lines 1-9:

> "...this invention provides a solid dosage form comprising cetirizine and pseudoephedrine, wherein at least a portion of said pseudoephedrine is contained in a core comprising said portion of pseudoephedrine, said core being surrounded by a permeable membrane, whereby release of said pseudoephedrine into an environment of use is sustained...:

Thus, the first dosage form has a drug core surrounded by a permeable membrane that controls release of drug from the core. An immediate release layer of the second drug cetirizine is coated on the permeable membrane (Col. 2, lines 8-9; Col. 2, lines 37-40). The drug core in this embodiment is an *immediate release* drug core, and release of drug is controlled by the water insoluble, drug permeable, rate-limiting membrane (Col. 4, lines 51-58).

The second dosage form design is described on Col. 2, lines 22-27:

> This invention further provides a process for making a solid dosage form containing cetirizine and pseudoephedrine, comprising coating a shaped sustained release core comprising pseudoepherine with an immediate release layer comprising cetirizine and a water soluble film forming polymer..."

Thus, the second dosage form design has a sustained release drug core surrounded by an immediate release layer of cetirizine.

These two alternative embodiments are also clearly and unequivocally set out in at least these passages of the '618 patent:

Col. 3, lines 17-27: For example, the pseudoephedrine can be incorporated into a sustained release matrix that meters pseudoephedrine out over a period of 4 to 36 hours, the matrix thus constituting the core. Alternatively, the pseudoephedrine core can comprise a shaped pseudoephedrine immediate release composition and a surrounding, rate limiting membrane which imparts sustained release behavior to the core.

> Col. 4, lines 51-61: As previously mentioned the core can be a matrix which meters out pseudoephedrine. Alternatively, the pseudoephedrine core can be formed from an immediate release, pseudoephedrine-containing composition which is surrounded by a water insoluble, permeable, rate-limiting membrane that provides for sustained release of pseudoephedrine by limiting the rate at which pseudoephedrine diffuses into the environment of use. The core is in turn coated over at least a portion of its surface with a layer comprising cetirizine and a water soluble film forming polymer that provides immediate release.

Accordingly, the '618 patent does not teach or suggest a dosage form having a prolonged release drug-containing core which is surrounded by a membrane or barrier layer which is water soluble and which dissolves in gastric fluid.

C. Analysis

In maintaining the rejection of claims 1-18 as unpatentable over the '618 patent, the Examiner makes several errors, some of which are addressed below.

C1. First Error: Misunderstanding and/or Misreading of the teachings in the '618 patent

The Examiner has misunderstood the disclosure of the '618 patent, and as a result has erroneously concluded that that the teachings of the '618 patent "differ[s] from the instant claims in disclosure of the ratio of unitary dosage from [sic, form] to the polymer film" (Final Office action dated February 19, 2010 (hereafter "Final Office action"), page 3, point 6). That is, the Examiner asserts that the '618 patent teaches a first drug formed into a solid matrix core which is coated with a polymer not comprising a drug, which is further coated with a drug formulation (Final Office action, page 3, point 5).

In these assertions, the Examiner's first error is in failing to understand that the '618 patent describes two separate and different dosage forms for sustained release of pseudoephedrine (see, for example, in the 618 patent, Col. 3, lines17-27; Col. 4, lines 51-63). As detailed above in section B, the first dosage form described in the '618 patent has an immediate release drug core surrounded by a permeable

membrane that controls release of drug from the core. An immediate release layer of the second drug cetirizine is coated on the permeable membrane (Col. 2, lines 8-9; Col. 2, lines 37-40). The drug core in this embodiment is an *immediate release* drug core, and release of drug is controlled by the water insoluble, drug permeable, rate-limiting membrane (Col. 4, lines 51-58; Col. 9, line 10 to Col. 10, line 7).

This embodiment obviously differs from the claimed dosage form in the type of drug core. In the '618 patent the core is an immediate release core, whereas in the claimed method of manufacture, the dosage form is fabricated to have a core (solid matrix to form a unitary body) that releases the drug by prolonged release (see claim 1, part (a)). Thus, this embodiment of the '618 patent does not teach a dosage form, nor a method of making same, that "differ[s] from the instant claims in disclosure of the ratio of unitary dosage from [sic, form] to the polymer film" as the Examiner asserts. Accordingly, there is a key structural difference between this embodiment in the '618 patent and the dosage form prepared by the claimed method - an immediate release core versus a prolonged release core. This embodiment of the '618 patent does not, therefore, show or suggest all of the features of the claimed method.

The second dosage form described in the '618 patent has a sustained release drug core coated with an immediate release layer of a second drug. This dosage form is clearly described in several places in the '618 patent, including Col. 2, lines 22-27; Col 3, lines 20-22 ("*...the pseudoephedrine can be incorporated into a sustained release matrix that meters pseudoephedrine out over a period of 4 to 36 hours...*"); see also Col. 6, line 57 to Col. 7, line 61). In this embodiment, the drug is "released both by diffusion from the matrix and by erosion of the matrix" (Col. 7, lines 14-15). Notably, there is no teaching or suggestion in the '618 patent that this embodiment, where the dosage form has a sustained release core, additionally includes a rate limiting membrane surrounding the sustained release core. This makes sense, since the sustained release core is designed to release the drug over a prolonged period of time and a rate limiting membrane covering the core is both (i) not needed to achieve sustained release and (ii) would alter the rate of release from the core.

Thus, a complete reading of the '618 patent informs the reader of two approaches to sustained release of a drug - an immediate release drug core

surrounded by a rate limiting membrane or a sustained release core, both of which include an immediate release coat of a second drug. Nowhere does the '618 patent suggest manufacture of a dosage form having a sustained release core coated with a drug-free polymer film that dissolves upon ingestion and another polymer-drug coating deposited on the drug-free polymer film.

In the brief discussion with the Examiner on May 14, 2010, the Examiner noted the passages on Col. 8, lines 18-24 and Col. 8, lines 25-33 as relevant to the claimed method. Applicants respectfully ask the Examiner to read entirely and completely the sections leading into these passages, beginning at Col. 6, line 57. At Col. 6, line 57, the '618 patent describes the sustained release core for release of the drug via diffusion from and erosion of the matrix. On Col. 7, line 3, the '618 patent lists hydrophilic materials for the sustained release core, referring on Col. 7, line 33 to the matrix as a "hydrogel matrix". On Col. 7, line 49, the '618 patent describes coating the sustained release matrix with an "impermeable coating" and including an orifice in the coating through which drug is release. The "impermeable coating" is described on Col. 8, lines 51-55 as one that has no significant transport of pseudoephedrine during the time scale of the intended drug release (41-36) hours.

The impermeable coating of the '618 patent remains intact during the period of drug release, hence the need for the hole or orifice in the coating to permit release of drug from the core. This type of impermeable coating is well known in the art and used in the well-described "osmotic dosage forms." In contrast, the claimed method is directed to the manufacture of a dosage form that has a sustained release core and a polymer film that *dissolves in gastrointestinal fluid upon ingestion.*

In summary, the Examiner has erred in maintaining the rejection on the grounds that the sole difference between the '618 patent and the claims is in the ratios of the unitary body and the polymer film, as set forth in the pending dependent claims.

C2. Second Error: Ignoring Words in the Claim

To support an obviousness rejection, MPEP §2143.03 requires "all words of a claim to be considered" and MPEP § 2141.02 requires consideration of the "[claimed] invention and prior art as a whole." Further, the Board of Patent Appeal and Interferences recently confirmed that a proper, post-KSR obviousness

determination still requires the Office make "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *In re Wada and Murphy*, Appeal 2007-3733, citing *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) and *CFMT v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003). It remains well-settled law that an obviousness rejection requires a suggestion of *all* of the claim elements.

In maintaining the rejection, the Examiner has not followed this well-settled law. In the Final Office action, on page 7, the Examiner states that:

> Applicant argues that the function of the instant invention differs from the '618 patent, since the sustained release core can function without a rate limiting film. This function is not however claimed. Again Applicant attempts to argue aspects of the invention that are not presently claimed.

This statement is puzzling. First, part (a) of claim 1 expressly recites:

> dispersing said second drug in a solid matrix to form a unitary body which upon immersion in a gastrointestinal fluid releases said second drug by prolonged release (emphasis added).

The claim includes as a positively recited feature that the solid matrix is a unitary body that releases the drug by prolonged release. When read in light of the specification, it is entirely clear that the unitary body/solid matrix itself provides prolonged release. Thus, the Examiner's statement is not understood since the pending claims absolutely state that the solid matrix release drug by prolonged release.

To the extent this statement by the Examiner is an invitation to specify that the solid matrix provides prolonged release in the absence of a rate-limiting membrane, Applicants urge reconsideration of this position. It is accepted practice to claim a method or composition by positively reciting the features and/or functions of the elements, and there is no requirement that claims itemize functions or features that an element does not need or is not capable of doing.

C3. Third Error: Misstatements in the Final Office action, suggesting a lack of understanding

On page 5 of the Final Office action, the Examiner agrees that "molecular weight, cross-linking, etc., can change a polymer's properties, yet none of these propertie4s [sic] have been claimed or recited anywhere in the instant claims or specification." "Applicant is arguing speculated element of the instant invention which are not present in the instant claims."

In response, the Examiner is directed to claim 1, part (b), where the claim expressly states "depositing on a surface of said unitary body a polymeric film that is devoid of either said first drug or said second drug, said polymeric film formed from a polymer (i) effective to prevent interaction of the second drug and the first drug prior to administration of the dosage form and (ii) which dissolves in gastrointestinal fluid upon ingestion.

By functionally specifying that the polymer film is formed of a polymer that dissolves in gastrointestinal fluid upon ingestion, and that prevents interaction of the first and second drugs prior to ingestion, the properties of the polymer are set forth. Obviously, polymers that do not dissolve or that are permeable to the first or second drug do not satisfy the requirements of claim 1(b). In this way, Applicants define the properties of the polymers, and it is therefore incorrect to state that Applicants argue element not present in the claims.

Second, in the passage in the Final Office action bridging pages 5-6, the Examiner refers to the impermeable membrane of the '618 patent and then goes on to refer to the drug-free membrane surrounding the sustained release body in the '618 patent as comprising leachable materials such as polyvinyl alcohol and semi-permeable materials such as cellulose acetate. Applicants respectfully point out that the Examiner is mixing up the various embodiments of the '618 patent. The impermeable membrane disclosed on Col. 8 is made of the thermoplastic polymers listed on Col. 9, lines 2-5, and the membrane has an exit hole through which "the majority of transport" occurs (Col. 9, lines 1-2). The teaching in the '618 patent with respect to polyvinyl alcohol and cellulose acetate is with respect to the rate limiting membrane coating an immediate release core, set forth on Col. 9, line 10-Col. 10, line 67. The Examiner is picking and choosing from unrelated embodiments in the '618 patent in an unsuccessful attempt to piece together the claimed method.

The Examiner asserts on page 6, line 5 of the Final Office action that "These components would form a film that dissolves in gastrointestinal fluid." This assertion is entirely unsubstantiated by evidence on the record, and is in fact incorrect. Cellulose acetate is not soluble in water, and therefore is not dissolvable in gastrointestinal fluid which is primarily water. If the Examiner can provide evidence to the contrary, Applicants extend an invitation to do so.

C4. Reiteration of the Applicant's Position: No Prima Facie Case of Obviousness

An obviousness analysis is informed by consideration of the factors stated in *Graham v. John Deere*, 383, U.S. 1, 148 USPQ 459 (1966). That is, the factors which must be considered in an inquiry directed to the obviousness or non-obviousness of an invention are as follows:

(i) scope and content of the asserted art

(ii) differences between claimed subject matter and the asserted art; and

(iii) the level of ordinary skill in the art.

In this analysis, the cited references must be viewed without the benefit of hindsight afforded by the claimed subject matter or accompanying specification.

From the comments in C1-C3 above, it is evident that the '618 patent fails to show or suggest each and every element of the claimed method. The Examiner has incorrectly taken the position that the '618 patent teaches a sustained release drug core surrounded by a drug-free polymer layer that dissolves and that has an immediate release drug layer over the drug-free polymer layer, and that since the '618 patent teaches the same dosage form, it also teaches the same method of manufacture. The primary error in this position is a failure to understand the teaching of the '618 patent. The '618 patent nowhere shows or suggests a sustained release core surrounded by a drug-free dissolvable polymer layer, for all the reasons given above. For this reason, the obviousness rejection cannot stand, and withdrawal is respectfully requested.

C5. Reiteration of Applicants' Position: The Modification to the Prior Art to Arrive at the dosage form made by the claimed method would render the prior art dosage form unsatisfactory for its intended function

In response to the arguments presented by Applicants in the November 9, 2009 response that the proposed modification would render the dosage form of the '618 patent unsatisfactory for its intended function, the Examiner notes that the only modifications proposed by the Examiner are those to optimize the ratios of the polymeric film to the unitary body, and the release rate of the first and second drug, which can be arrived upon through routine experimentation.

In response, Applicants reiterate their position that modification of the dosage forms in the '618 patent to arrive at the dosage form prepared according to the claimed method would render the dosage form of the '618 patent inoperable for its intended function of sustained drug release. Specifically, to arrive at the instant claims, it would be required to include a dissolvable film on the sustained release matrix of the '618 patent dosage form. This modification is completely unnecessary based on the teachings in the '618 patent, since in the dosage form taught in the '618 patent the matrix provides the sustained release and there is no rational basis to assert that a dissolvable polymer film should be deposited on the sustained release matrix, nor is such a film taught or suggested by the '618 patent. The embodiment in the '618 patent where the dosage form has an immediate release core includes a semi-permeable membrane that remains intact after ingestion since the membrane provides the sustained release feature of the dosage form.

In light of the arguments presented above, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a).

IV. Conclusion

Claims 1-18 are believed to satisfy all of the criteria for patentability and are in condition for Allowance. An early indication of the same is therefore kindly requested.

No fees are believed to be due in connection with this Response. However, the Commissioner is authorized to charge any additional fees that may be required, or credit any overpayment, to King & Spalding LLP Deposit Account No. 50-4616.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 590-0734.

Respectfully submitted,
King & Spalding LLP

Date: May 24, 2010

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